Melorheostosis

Melorheostosis is a rare bone disease. It causes the abnormal growth of new bone tissue on the surface of existing bones. The new bone has a characteristic appearance on x-rays, often described as "flowing" or like dripping candle wax. The excess bone growth typically occurs on the bones in one arm or leg, although it can also affect the pelvis, breastbone (sternum), ribs, or other bones. (The term "melorheostosis" is derived from the Greek words "melos," which means limb; "rheos," which means flow; and "ostosis," which refers to bone formation.) The abnormal bone growth associated with melorheostosis is noncancerous (benign), and it does not spread from one bone to another.

The signs and symptoms of melorheostosis usually appear in childhood or adolescence. The condition can cause long-lasting (chronic) pain, permanent joint deformities (contractures), and a limited range of motion of the affected body part. In some people, the limb may appear thickened or enlarged, and the skin overlying the affected area can become red, thick, and shiny.

Another rare disease, Buschke-Ollendorff syndrome, can include melorheostosis. Buschke-Ollendorff syndrome is characterized by skin growths called connective tissue nevi and areas of increased bone density called osteopoikilosis. A small percentage of affected individuals also have melorheostosis or other bone abnormalities. Scientists originally speculated that melorheostosis that occurs without the other features of Buschke-Ollendorff syndrome might have the same genetic cause as that syndrome. However, it has since been determined that Buschke-Ollendorff syndrome and melorheostosis that occurs alone are caused by mutations in different genes, and the two conditions are considered separate disorders.

Frequency

Melorheostosis affects about 1 in 1 million people. Approximately 400 cases have been reported worldwide.

Causes

Mutations in the *MAP2K1* gene are estimated to cause about half of all cases of melorheostosis. The *MAP2K1* gene provides instructions for making a protein called MEK1 protein kinase. This protein is active in many kinds of cells, including bone cells. It is part of a signaling pathway called RAS/MAPK. This signaling pathway helps control the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), and cell movement (migration). RAS/MAPK signaling is critical for normal development, including the formation of bones.

The *MAP2K1* gene mutations that cause melorheostosis are somatic, which means that they occur during a person's lifetime and are present only in certain cells, in this case, bone cells in a particular area of the body. The mutations lead to the production of a version of MEK1 protein kinase that is overactive, which increases RAS/MAPK signaling in bone tissue. The increased signaling disrupts the regulation of bone cell proliferation, allowing new bone to grow abnormally. Studies suggest that increased RAS/MAPK signaling also stimulates excess bone remodeling, a normal process in which old bone is broken down and new bone is created to replace it. These changes in bone growth and turnover underlie the bone abnormalities characteristic of melorheostosis.

In cases of melorheostosis without an identified mutation in the *MAP2K1* gene, the cause of the condition is usually unknown. Studies suggest that somatic mutations in other genes, particularly genes related to the RAS/MAPK signaling pathway, may also cause the disorder.

Inheritance Pattern

This condition is not inherited from a parent, and it cannot be passed down to children. It arises from somatic mutations in bone cells that occur during an individual's lifetime.

Other Names for This Condition

- candle wax disease
- flowing hyperostosis
- hyperostosis, monomelic
- Leri syndrome
- Leri's disease
- melorheostoses
- melorheostosis of Leri
- melorheostosis, isolated
- periostitis; monomelic
- rheostosis

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Melorheostosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3149631/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22melorheostosis%22

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html

Genetic and Rare Diseases Information Center

- Melorheostosis
  https://rarediseases.info.nih.gov/diseases/9474/melorheostosis

Educational Resources

- MalaCards: melorheostosis
  https://www.malacards.org/card/melorheostosis
- NIH News Release: NIH Researchers Crack Mystery Behind Rare Bone Disorder (April 11, 2018)
  https://www.nih.gov/news-events/news-releases/nih-researchers-crack-mystery-behind-rare-bone-disorder
- Orphanet: Melorheostosis
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2485

Patient Support and Advocacy Resources

- Melorheostosis Association
  http://www.melorheostosis.com/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/melorheostosis/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Melorheostosis%5BMAJR%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- MELORHEOSTOSIS, ISOLATED
  http://omim.org/entry/155950

Medical Genetics Database from MedGen

- Melorheostosis
  https://www.ncbi.nlm.nih.gov/medgen/7525

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